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L MOLECULES OF THE PYRIN DOMAIN PROFAMILY AND USES THEREOF

CAGC TGGT					C GA	GTAG	GGCC	AGG	TGTT	GGG	AGCT	CCCA	CG T	GGGA	CAAGG	60 77
atg Met 1	g gt Gly	ttc Phe	aac Asn	ctg Leu 5	c ag Gln	gct Ala	ctc Leu	ctg Leu	gag GLu 10	cag Gln	ctc Leu	agc Ser	cag Gln	gat Asp 15	g ag Glu	125
ttg Leu	agc Ser	aag Lys	ttc Phe 20	aag Lys	tat Tyr	ctg Leu	atc Ile	acg Thr 25	acc Thr	ttc Phe	tcc Ser	ccg Pro	gca Ala 30	ca c His	g ag Glu	173
ctc Leu	cag Gln	aag Lys 35	atc Ile	ccc Pro	cac His	aag Lys	gag Glu 40	gta Val	gac Asp	aag Ly s	gct Ala	gat Asp 45	ggg Gly	aag Lys	caa Gln	2 21
ctg Leu	gta Val 50	g aa Glu	atc Ile	ctc Leu	acc Thr	acc Thr 55	cat His	tgt Cys	gac Asp	agc Ser	tac Tyr 60	tgg Trp	gtg Val	ga g Glu	atg M et	269
gcg Ala 65	agc Ser	ctc Leu	cag Gln	gtc Val	ttt Phe 70	gaa Glu	aag Lys	atg Met	cac His	cga Arg 75	atg Met	gat Asp	ctg Leu	tct Ser	gag Glu 80	317
ag a Arg	gca Ala	aag Lys	gat Asp	gaā Glu 85	gtc Val	aga Arg	gaa Glu	gca Ala	gct Ala 90	ttg Leu	a aa Lys	tcc Ser	ttt Phe	aat Asn 95	a aa Lys	365
agg Arg	aag Lys	cct Pro	cta Leu 100	tca Ser	tta Leu	ggg Gly	ata Ile	aca Thr 105	cgg Arg	aaa Lys	gaa Glu	cga Arg	cca Pro 110	cct Pro	cta Leu	413
g ac Asp	gtg Val	gac Asp 115	g aa Glu	atg Met	ctg Leu	gag Glu	cgc Arg 120	ttc Phe	aaa Lys	aca Thr	gaa Glu	gca Ala 125	caa Gln	gac Asp	aaa Lys	461
gac Asp	aat Asn 130	agg Arg	tgc Cy s	agg Arg	tat Tyr	ata Ile 135	ttg Leu	aag Lys	acg Thr	aag Lys	ttc Phe 140	cgg Arg	gag Glu	atg M e t	tgg Trp	509
aag Lys 145	agc Ser	tgg Trp	cct Pro	gga Gly	gat Asp 150	agc Ser	aaa Lys	gag Glu	gtc Val	cag Gln 155	gtt Val	atg M et	gct Ala	gag Glu	aga Arg 160	557
tac T <u>yr</u>	aag Lys	atg Met	ctg Leu	atc Ile 165	Pro	ttt Phe	agc Ser	aac Asn	ecc Pro 170	Arg	g gtg g Val	ctt Leu	cac Pro	ggg Gly 175	Pro	605
ttc Phe	tca Ser	tac Tyr	acg Thr 180	gtg Val	gtg Val	ctg Leu	tat Tyr	ggt Gly 185	Pro	gca Ala	a ggc a Gly	ctt Leu	ggg 1 Gl ₃ 190	/ Lys	acc Thr	653
acg Thr	ctg Leu	gcc Ala 195	cag Gln	aaa Lys	cta Leu	atg Met	cta Leu 200	. Asp	tgg Trp	gca Ala	a gag a Glu	gad Asp 205	Asr	cto Lei	atc l Ile	701

FIG. 1A

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NOVE MOLECULES OF THE PYRIN DOMAIN PROTEIN FAMILY AND USES THEREOF

cac His	aaa Lys 210	ttc Phe	aaa Lys	nat Tyr	gcg Ala	ttc Phe 215	tac Tyr	ctc Leu	agc Ser	cāc Cāc	agg Arg 220	g ag Glu	ctc Leu	agc Ser	cgc Arg	749
ctg Leu 225	ggc Gly	ccg Pro	tgc Cys	agt Ser	Phe 230	gca Ala	gag Glu	ctg Leu	gtc Val	ttc Phe 235	agg Arg	gac A sp	tgg Trp	cct Pro	gaa Glu 240	797
ttg Leu	cag Gln	gat Asp	gac Asp	att Ile 245	cca Pro	cac His	atc Ile	cta Leu	gcc Ala 250	caa Gln	gca Ala	cąg Arg	aaa Lys	atc Ile 255	ttg Leu	845
ttc Phe	gtg Val	att Ile	gac Asp 260	ggc Gly	ttt Phe	Jat Asp	gag Glu	ctg Leu 265	gga Gly	gcc Ala	gca Ala	cct Pro	ggg Gly 270	gcg Ala	ctg Leu	893
atc Ile	gag Glu	gac Asp 275	atc -Ile	tgc Cys	gg g	gac Asp	tgg Trp 280	gag Glu	aag Lys	aag Lys	aag Lys	ccg Pro 285	gtg Val	ccc Pro	gtc Val	941
ctc Leu	ctg Leu 290	gg g	agt Ser	ttg Leu	ctg Leu	aac Asn 295	agg Arg	gtg Val	atg Met	tta Leu	ccc Pro 300	aag Lys	gcc Ala	gcc Ala	ctg Leu	9 89
ctg Leu 305	gtc Val	acc Thr	acg Thr	cgg Arg	ccc Pro 310	agg Arg	gcc Ala	ctg Leu	agg Arg	gac Asp 315	ctc Leu	cgg Arg	atc Ile	ctg Leu	gcg Ala 320	1037
g ag Glu	gag Glu	ccg Pro	atc Ile	tac Tyr 325	ata Ile	agg Arg	gtg Val	gag Glu	ggc Gly 330	ttc Phe	ctg Leu	gag Glu	gag Glu	gac Asp 335	aag Lys	1085
agg Arg	gcc Ala	tat Tyr	ttc Phe 340	ctg Leu	aga Arg	cac His	ttt Phe	gga Gly 345	gac Asp	gag Glu	gac Asp	caa Gln	gcc Ala 350	Met	cgt Arg	1133
gc c Ala	ttt Phe	gag Glu 355	Leu	atg Met	agg Arg	agc Ser	aac Asn 360	Ala	gcc Ala	ctg Leu	tto Phe	cag Gln 365	Leu	r Glř i äác	tcg Ser	1181
gcc Ala	ccc Pro 370	Ala	gtg Val	tgc Cys	tgg Trp	atc Ile 375	gtg Val	tgc Cys	acg Thr	act Thr	cto Lev 380	ı Lys	r ctq Lev	g caç ı Glr	atg Met	1229
g ag Glu 3 85	Lys	ggg Gly	gag Glu	gac Asp	ccg Pro 390	Val	ccc Pro	acc Thr	tgc Cys	cto Leu 395	ı Thi	c cgc	acq Thi	g ggg	g ctg y Leu 400	1277
tto Phe	ctg Leu	cgt Arg	ttc Phe	Leu 405	Cys	agc Ser	cgg Arg	r tto Phe	e ccc Pro 410	Glr	g ggd n Gly	e gca y Ala	a caq a Gli	g cto Let 41:	g cgg 1 Arg	1325
g gc Gly	gcg Ala	ctg Leu	cgg Arg 420	Thr	r ctg : Leu	agc Ser	cto Leu	cto Leu 425	ıAla	e geo	g cad a Gli	g ggo n Gly	c cto y Lei 430	ı Tr	g gcg p Ala	1373

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		tcc Ser 435														1421
		gac Asp														1469
aga Arg 465	gtc Val	tcc Ser	aaa Lys	ggc Gly	tgc Cys 470	tac Tyr	tcc Ser	ttc Phe	atc Ile	cac His 475	ctc Leu	agc Ser	ttc Phe	cag Gln	cag Gln 480	1517
		act Thr														1565
		g gc Gly														1613
g ga Gly	gta Val	gaa Glu 515	aga Arg	ctc Leu	agg Arg	aac Asn	ccc Pro 520	gac Asp	ctg Leu	atc Ile	caa Gln	gca Ala 525	ggc Gly	tac Tyr	tac Tyr	1661
tcc Ser	ttt Phe 530	gg c Gly	ctc Leu	gct Ala	aac Asn	gag Glu 535	aag Lys	aga Arg	gcc Ala	aag Lys	gag Glu 540	ttg Leu	gag Glu	gcc Ala	act Thr	1709
		tgc Cys													Cys	1757
343					220					333					560	
gac	ata Ile	agt Ser	tgt Cys	aag Lys 565	ggt	gga Gly	cat His	tca Ser	acg Thr 570	gtg	aca Thr	gac Asp	ctg Leu	cag Gln 575	gag	1805
gac Asp	Ile	agt Ser ggc Gly	Cys	Lys 565 ctg	ggt Gly tac	Gly gag	His	Ser	Thr 570 gag	gtg Val gag	Thr	Asp	Leu gtg	Gln 575 aag Lys	gag Glu gag	1805
gac Asp stc Leu	Ile ctc Leu	ggc Gly gct	tgt Cys 580	Lys 565 ctg Leu ttc	ggt Gly tac Tyr	gag Glu gaa	His tct Ser	cag Gln 585	Thr 570 gag Glu ctg	gtg Val gag Glu	Thr gag Glu tta	Asp ctg Leu	gtg Val 590 gca Ala	Gln 575 aag Lys gta	gag Glu gag Glu	
gac Asp etc Leu gtg Val	Ile ctc Leu atg Met	ggc Gly gct Ala 595	Cys tgt Cys 580 cag Gln	Lys 565 ctg Leu ttc Phe	ggt Gly tac Tyr aaa Lys	gag Glu gaa Glu	His tct Ser ata Ile 600	cag Gln 585 tcc Ser	Thr 570 gag Glu ctg Leu	gtg Val gag Glu cac His	Thr gag Glu tta Leu cga	Asp ctg Leu aat Asn 605 aac	gtg Val 590 gca Ala	Gln 575 aag Lys gta Val	gag Glu gag Glu	1853
gac Asp ctc Leu gtg Val gtt Val	ctc Leu atg Met gtg Val 610	ggc Gly gct Ala 595 cca Pro	tgt Cys 580 cag Gln tct Ser	Lys 565 ctg Leu ttc Phe tca Ser	ggt Gly tac Tyr aaa Lys ttc Phe	gag Glu gaa Glu tgc Cys 615	tct Ser ata Ile 600 gtc Val	cag Gln 585 tcc Ser aag Lys	Thr 570 gag Glu ctg Leu cac His	gtg Val gag Glu cac His tgt Cys	Thr gag Glu tta leu cga Arg 620 gag Glu	Asp ctg Leu aat Asn 605 aac Asn	gtg Val 590 gca Ala	Gln 575 aag Lys gta Val	gag Glu gag Glu gac Asp	1853 1901

ACCIONATE PAGE 10 ACCIONATE PA

ctt Leu	cct Pro	ttc Phe	tgg Trp 660	acg Thr	gac Asp	ctt Leu	tg t Cys	tee Ser 665	ata Ile	ttt Phe	gga Gly	tca Ser	aat Asn 670	aag Lys	gat Asp	2093
ctg L eu	atg Met	ggt Gly 675	cta Leu	gca Ala	atc Ile	aat Asn	gat Asp 680	agc Ser	ttt Phe	ctc Leu	agt Ser	gcc Ala 685	toc Ser	cta Leu	gta Val	2141
agg Arg	atc Ile 690	ctg Leu	tgt Cys	ga a Glu	caa Gln	ata Ile 695	gcc Ala	tot Ser	gac Asp	acc Thr	tgt Cys 700	cat His	ctc Leu	cag Gln	aga Arg	2189
gtg Val 705	gtg Val	ttc Phe	a aa Lys	aac Asn	att Tle 710	tcc Ser	cca Pro	gct Ala	g at Asp	gct Ala 715	cat His	cgg Arg	aac Asn	ctc Leu	tgc Cys 720	2237
cta Leu	gct Ala	ctt Leu	cga Arg	ggt Gly 725	cac His	aag Lys	act Thr	gta Val	acg Thr 730	tat Tyr	ctg Leu	acc Thr	ctt Leu	caa Gln 735	ggc Gly	2285
aat Asn	gac Asp	cag Gln	gat Asp 740	gat Asp	atg Met	ttt Phe	ccc Pro	gca Ala 745	ttg Leu	tgt Cys	g ag Glu	gtc Val	ttg Leu 750	aga Arg	cat His	2333
cca Pro	gaa Glu	tgt Cys 755	aac Asn	ctg Leu	cga Arg	tat Tyr	ctc Leu 760	gg g Gly	ttg Leu	gtg Val	tct Ser	tgt Cys 765	tcc Ser	gct Ala	acc Thr	2381
act Thr	cag Gln 770	cag Gln	tgg Trp	gct Ala	gat Asp	ctc Leu 775	tcc Ser	ttg Leu	gcc Ala	ctt Leu	gaa Glu 780	gtc Val	aac Asn	cag Gln	tcc Ser	2429
ctg Leu 785	acg Thr	tgc Cys	gta Val	aac Asn	ctc Leu 790	tcc Ser	gac Asp	aat Asn	g ag Glu	ctt Leu 795	ctg Leu	gat Asp	gag Glu	ggt Gly	gct Ala 800	2477
aag Lys	ttg Leu	ctg Leu	tac Tyr	aca Thr 805	act Thr	ttg Leu	aga Arg	cac Hıs	ccc Pro 810	aag Lys	tgc Cys	ttt Phe	ctg Leu	cag Gln 815	agg Arg	2 525
ttg Leu	tcg Ser	ttg Leu	gaa Glu 820	aac Asn	tg t Cys	cac His	ctt Leu	aca Thr 825	gaa Glu	gcc Ala	aat Asn	tgc Cys	aag Lys 830	gac Asp	ctt Leu	2573
gct Ala	gct Ala	gtg Val 835	ttg Leu	gtt Val	gtc Val	agc Ser	cgg Arg 840	gag Glu	ctg Leu	aca Thr	cac His	ctg Leu 845	tgc Cys	ttg Leu	gcc Ala	2621
aag Lys	aac Asn 850	ccc Pro	att Ile	ggg Gly	aat Asn	aca Thr 855	GJ Y gg g	gtg Val	aag Lys	ttt Phe	ctg Leu 860	tg t Cys	gag Glu	ggc Gly	ttg Leu	2669
											ctt Leu					2717

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FAMILY AND USES THEREOF

ata a	act Thr	agc Ser	gat Asp	ggc Gly 885	tgc Cys	tgc Cys	gat Asp	ctc Leu	aca Thr 890	aag Lys	ctt Leu	ctc Leu	caa Gln	gaa Glu 895	aaa Lys	2765
tca a	agc Ser	Leu ctā	ttg Leu 900	tgt Cys	ttg Leu	gat Asp	ctg Leu	ggg Gly 905	ctg Leu	aat Asn	cac His	ata Ile	gga Gly 910	gtt Val	aag Lys	2813
g ga (Gly (atg Me t	aag Lys 915	ttc Phe	ctg Leu	tgt .Cys	gag Glu	gct Ala 920	ttg Leu	agg Arg	aaa Lys	cca Pro	ctg Leu 925	tgc Cys	aac Asn	ttg Leu	2861
aga Arg	tgt Cys 9 30	ctg Leu	tgg Trp	ttg Leu	tgg Trp	gga Gly 935	tgt Cys	tcc Ser	atc	cct Pro	ccg Pro 940	ttc Phe	agt Ser	tgt Cys	ga a Glu	29 09
gac Asp 945	ctc Leu	tgc Cys	tct Ser	gc c Ala	ctc Leu 950	agc Ser	aac Asn	cag Gln	agc Ser	ctc Leu 955	gtc Val	act Thr	ctg Leu	gac Asp	ctg Leu 960	2957
ggt Gly	cag Gln	aat Asn	ccc Pro	ttg Leu 9 65	GJ À āđā	tc t Ser	agt Ser	gga Gly	gtg Val 970	aag Lys	atg Met	ctg Leu	ttt Phe	gaa Glu 975	Thr	3005
ttg Leu	aca Thr	tgt Cys	tcc Ser 980	agt Ser	ggc Gly	acc Thr	ctc Leu	cgg Arg 985	Thr	ctc Leu	agg Arg	ttg Leu	aaa Lys 990	Ile	gat Asp	3053
gac Asp	ttt Phe	aat Asn 99	Asp	gaa Glu	ctc Leu	aat Asn	aag Lys 100	Leu	ctg Leu	gaa Glu	gaa Glu	ata Ile 100	Glu	gaa Glu	aaa Lys	3101
aac Asn	cca Pro 101	Gln	ctg Leu	att Ile	att Ile	gat Asp 101	Thr	gag Glu	aaa Lys	cat His	cat His 102	Pro	tgg Trp	g gca Ala	ı gaa ı Glu	3 149
agg Arg 1025	Pro	tct Ser	tct Ser	cat His	gac Asp 103	Phe	atq Met	ato : Ile	:							3176
TGCC GCTA TTAC	CTGT AGAT CATA	GAC GTT TGA	TCCT	CTCC CCAT TCTG	TC C	CCGG	CCCC	T AC	CCCT	CAGO	GA:	CAAT(CACA(SAGT	TCA	EGTGAAC ITGCTGG ATCTTTG CATTCAC	3236 3296 3356 3416 3431

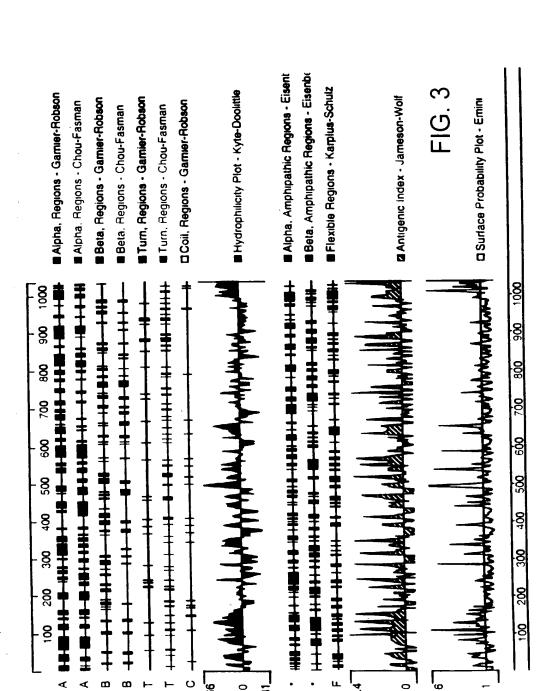
FIG. 1E

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cant(s): John Bertin et al.
NOVEL MOLECULES OF THE PYRIN DOMAIN PROTEIN
FAMILY AND USES THEREOF

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FAMILY AND USES THEREOF

ccacgcgtcc go cactcctgga to aaacagctgc ao	cgagccaac agg gatgaag atg g	gagaactt tct gca agc acc	gtgtgga (cgc tgc (ttetteeatg ge cegaageeta ag aag etg gee a Lys Leu Ala A	gaccctga gg tac	60 120 171
ctg gag gac Leu Glu Asp	ctg gag gat g Leu Glu Asp \ 15	gtg gac ttg /al Asp Leu 20	aag aaa Lys Lys	ttt aag atg o Phe Lys Met F . 25	ac tta His Leu	219
gag gac tat Glu Asp Tyr 30	cct ccc cag a Pro Pro Gln I	aag ggc tgc Lys Gly Cys 35	atc ccc Ile Pro	ctc ccg agg (Leu Pro Arg (40	ggt cag Gly Gln	267
aca gag aag Thr Glu Lys 45	gca gac cat o Ala Asp His V	gtg gat cta Val Asp Leu 50	gcc acg Ala Thr	cta atg atc of Leu Met Ile i	gac ttc Asp Phe	315
aat ggg gag Asn Gly Glu 60	gag aag gcg f Glu Lys Ala 7 65	tgg gcc atg Irp Ala Met	gcc gtg Ala Val 70	tgg atc ttc o	gct gcg Ala Ala 75	363
atc aac agg Ile Asn Arg	aga gac ctt ' Arg Asp Leu ' 80	tat gag aaa Tyr Glu Lys	gca aaa Ala Lys 85	aga gat gag Arg Asp Glu	ccg aag Pro Lys 90	411
tgg ggt tca Trp Gly Ser	gat aat gca Asp Asn Ala 95	cgt gtt tcg Arg Val Ser 100	aat ccc Asn Pro	act gtg ata Thr Val Ile 105	tgc cag Cys Gln	459
gaa gac agc Glu Asp Ser 110	att gaa gag Ile Glu Glu	gag tgg atg Glu Trp Met 115	ggt tta Gly Leu	ctg gag tac Leu Glu Tyr 120	ctt tcg Leu Ser	507
aga atc tct Arg Ile Ser 125	att tgt aaa Ile Cys Lys	atg aag aaa Met Lys Lys 130	gat tac Asp Tyr	cgt aag aag Arg Lys Lys 135	tac aga Tyr Arg	555
aag tac gtg Lys Tyr Val 140	aga agc aga Arg Ser Arg 145	ttc cag tgc Phe Gln Cys	att gaa Ile Glu 150	gac agg aat Asp Arg Asn	gcc cgt Ala Arg 155	603
ctg ggt gag Leu Gly Glu	agt gtg agc Ser Val Ser 160	ctc aac aaa Leu Asn Lys	cgc tac Arg Tyr 165	aca cga ctg Thr Arg Leu	cgt ctc Arg Leu 170	651
atc aag gag Ile Lys Glu	cac cgg agc His Arg Ser 175	cag cag gag Gln Gln Glu 180	Arg Glu	cag gag ctt Gln Glu Leu 185	ctg gcc Leu Ala	699
atc ggc aag Ile Gly Lys 190	acc aag acg Thr Lys Thr	tgt gag agc Cys Glu Ser 195	ccc gtg Pro Val	agt ccc att Ser Pro Ile 200	aag atg Lys Met	747
gag ttg ctg Glu Leu Leu 205	ttt gac ccc Phe Asp Pro	gat gat gag Asp Asp Glu 210	g cat tct n His Ser	gag cct gtg Glu Pro Val 215	cac acc His Thr	795

FIG. 4A

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-	gtg Val		_			_							_	_		843	
	atg Met	_	-	-		-	-						-			891	
	tat Tyr															939	
	agc Ser	-		_	-		_	-	_	-		_				987	
	atc Ile 285															1035	
	ggc Gly															1083	
	tgc Cys		_		-	_	-				_			-	_	1131	
_	ctc Leu		_	-	-	_				_		_				1179	
-	aga Arg			-	_			_	_			_	_			1227	
, ,	cat His 365		_		_					_						1275	
															agt Ser 395	1323	
															ctg Leu	1371	
									Lys					Ser	ggc	1419	
													Tyr		ttc Phe	1467	

FIG. 4B

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App (s): John Bertin et al.

NO MOLECULES OF THE PYRIN DOMAIN PROTEINFAMILY AND USES THEREOF

	ctt Leu 445															1515
	tgc Cys	_						-		-	-	-	-			1563
	aac Asn															1611
_	cag Gln	-		-			-		-		-		-			1659
	gaa Glu															1707
	gag Glu 525															1755
	agg Arg															1803
	aca Thr	•		_	-						-	_			_	1851
att	ttt	att	ata	cat	ttc	ctc	ttt	aac	cta	gta		cag	gag	agg	acc	1899
Ile	Phe	-	-	-	Phe	Leu	Phe		_	-	Asn	Gln	Glu 585	Arg	Thr	1033
tcc	Phe	Val ttg	Val 575 gag	Arg	aaa	tta	agt	Gly 580 tgc	Leu	Val	tct	cag	585 caa	atc	Thr agg Arg	1947
tcc Ser ctg	Phe tac Tyr	Val ttg Leu 590	Val 575 gag Glu ctg	Arg aag Lys aaa	aaa Lys tgg	tta Leu att	agt Ser 595 gaa	Gly 580 tgc Cys	Leu aag Lys	Val atc Ile gcc	tct Ser aaa	cag Gln 600 gct Ala	585 caa Gln	atc Ile	agg	
tcc Ser ctg Leu	tac Tyr gag Glu 605 atc	Val ttg Leu 590 ctg Leu cag	Val 575 gag Glu ctg Leu	aag Lys aaa Lys	aaa Lys tgg Trp	tta Leu att Ile 610	agt Ser 595 gaa Glu	Gly 580 tgc Cys gtg Val	Leu aag Lys aaa Lys	Val atc Ile gcc Ala	tct Ser aaa Lys 615	cag Gln 600 gct Ala	585 caa Gln aaa Lys	atc Ile aag Lys	agg Arg ctg Leu	1947
tcc Ser ctg Leu cag Gln 620	tac Tyr gag Glu 605 atc Ile	ttg Leu 590 ctg Leu cag Gln	Val 575 gag Glu ctg Leu ccc Pro	aag Lys aaa Lys agc Ser	aaa Lys tgg Trp cag Gln 625	tta Leu att Ile 610 ctg Leu	agt Ser 595 gaa Glu gaa Glu	Gly 580 tgc Cys gtg Val ttg Leu	aag Lys aaa Lys ttc Phe	atc Ile gcc Ala tac Tyr 630 gac	tct Ser aaa Lys 615 tgt Cys	cag Gln 600 gct Ala ttg Leu	585 caa Gln aaa Lys tac Tyr	atc Ile aag Lys gag Glu	agg Arg Ctg Leu atg Met 635 att	1947 1995

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att Ile	gag Glu	aac Asn 670	tgt Cys	cat His	cgg Arg	gtg Val	gag Glu 675	tca Ser	ctg Leu	tcc Ser	ctg Leu	ggg Gly 680	ttt Phe	ctc Leu	cat His	2187
aac Asn	atg Met 685	ccc Pro	aag Lys	gag Glu	gaa Glu	gag Glu 690	gag Glu	gag Glu	gaa Glu	aag Lys	gaa Glu 695	ggc Gly	cga Arg	cac His	ctt Leu	2235
gat Asp 700	atg Met	gtg Val	cag Gln	tgt Cys	gtc Val 705	ctc Leu	cca Pro	agc Ser	tcc Ser	tct Ser 710	cat His	gct Ala	gcc Ala	tgt Cys	tct Ser 715	2283
cat His	gga Gly	ttg Leu	gtg Val	aac Asn 720	agc Ser	cac His	ctc Leu	act Thr	tcc Ser 725	agt Ser	ttt Phe	tgc Cys	cgg Arg	ggc Gly 730	ctc Leu	2331
ttt Phe	tca Ser	gtt Val	ctg Leu 735	agc Ser	acc Thr	agc Ser	cag Gln	agt Ser 740	cta Leu	act Thr	ga a Glu	ttg Leu	gac Asp 745	ctc Leu	agt Ser	2379
gac Asp	aat Asn	tct Ser 750	ctg Leu	ggg	gac Asp	cca Pro	ggg Gly 755	atg Met	aga Arg	gtg Val	ttg Leu	tgt Cys 760	gaa Glu	acg Thr	ctc Leu	2427
cag Gln	cat His 765	Pro	ggc Gly	tgt Cys	aac Asn	att Ile 770	cgg Arg	aga Arg	ttg Leu	tgg Trp	ttg Leu 775	Gly	cgc Arg	tgt Cys	ggc Gly	2475
ctc Leu 780	Ser	cat His	gag Glu	tgc Cys	tgc Cys 785	ttc Phe	gac Asp	atc Ile	tcc Ser	ttg Leu 790	Val	ctc Leu	agc Ser	agc Ser	aac Asn 795	2523
cag Gln	aag Lys	ctg : Leu	gtg Val	gag Glu 800	Leu	gac Asp	ctg Leu	agt Ser	gac Asp 805	Asn	gcc	cto Lev	ggt Gly	gac Asp 810	ttc Phe	2571
gga Gly	ato Ile	aga Arg	ctt Leu 815	Leu	tgt Cys	gtg Val	gga Gly	ctg Leu 820	Lys	cac His	cto Leu	g tto 1 Leu	tgc Cys 825	Ası	ctg Leu	2619
aaq Lys	g aag Lys	cto Lev 830	1 Trp	tto Lev	gtc Val	agc Ser	tgc Cys 835	Cys	cto Lev	aca Thr	tca Sei	a gca c Ala 840	a Cys	tgt GCys	cag s Gln	2667
gat Asp	ctt Lei 845	ı Ala	ı tca ı Ser	gta Val	ı ttg Leu	ago Ser 850	Thr	ago Ser	cat His	tco Sei	c cto Lev 85	u Thi	e aga r Arq	a cte	c tat u Tyr	2715
gto Val 860	l Gl	g gaq y Glu	g aat 1 Asr	gco Ala	tto Lev 865	Gly	gad Asp	c tca o Ser	gga Gly	a gto y Val 870	l Al	a at a Il	t tt: e Le:	a tg u Cy	t gaa s Glu 875	2763
aaa Ly:	a gco s Ala	c aad a Ly:	g aat s Asr	cca Pro 880	o Glr	ı tgt L Cys	aad Asi	c ctq n Lei	g cad 1 Gli 88	n Ly	a ct s Le	g gg u Gl	g tt y Le	g gt u Va 89	g aat 1 Asn 0	2811

FIG. 4D

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tct Ser	ggc Gly	ctt Leu	acg Thr 895	tca Ser	gtc Val	tgt Cys	tgt Cys	tca Ser 900	gct Ala	ttg Leu	tcc Ser	tcg Ser	gta Val 905	ctc Leu	agc Ser	2859
	aat Asn															2907
gac Asp	aag Lys 925	Gly	atc Ile	aaa Lys	cta Leu	ctc Leu 930	tgt Cys	gag Glu	gga Gly	ctc Leu	ttg Leu 935	cac His	ccc Pro	gac Asp	tgc Cys	2955
	ctt Leu															3003
	tgg Trp															3051
ctg Leu	agc Ser	ctg Leu	ggc Gly 975	aac Asn	aat Asn	gac Asp	ctg Leu	ggc Gly 980	gac Asp	ctg Leu	ggg Gly	gtc Val	atg Met 985	atg Met	ttc Phe	3099
tg t Cys	gaa Glu	gtg Val 99	Leu	aaa Lys	cag Gln	cag Gln	agc Ser 99	Cys	ctc Leu	ctg Leu	cag Gln	aac Asn 100	Leu	ggg	ttg Leu	3147
	gaa Glu 100	Met					Glu					Leu				3195
	gaa Glu O					Leu					Glu					3243
ggt gtg acg ctt ttc cag ttt	ggag tcgg ccag tcag tctt tgtt aact ttgt	aga aga ttat tac tagt aat	gctg agagg gagg tttt tttac agtt atgt	cgat agct aaga atgt ctct gctc tata ttgt	cc a c c c c c c c c c c c c c c c c c	tcca cgac cagg tctt ctgt tcat tatg ctaa	ggcc gatg acaa ggtg ctaa catt ttga taag	a agct ga cc cc cc a aa	acca tcct cagc tcat tctt gcta ttta aatc	cage gtge ateg gtaa ttte actt tgge catg	tct aga ggt tta cta tct agc	gtga gctt gttg gctc tctt atta tatt	tcc ggg ttc att ttt act tat ttat	ttee cate teat caat ttet gace ttat	ecctca eggtgga etccttt cacagc aaagca etctttg eataaca ettaaat gttgaaa	3303 3363 3423 3483 3543 3603 3663 3723 3783 3843 3857

FIG. 4E

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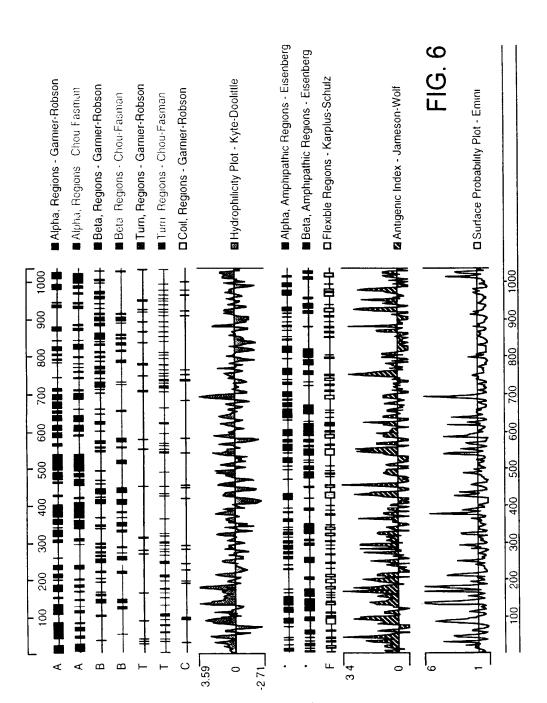
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Majority	Q K H H K E V D NBS1-PYRIN DOMAIN S I Q PYRIN-PYRIN DOMIAN G E I P A L L CARD5-PYRIN DOMAIN G E I P A P E CARD7-PYRIN DOMAIN	Majority	NES1-PYRIN DOMIN PYRIN-PYRIN DOMIAN CARD5-PYRIN DOMAIN CARD7-PYRIN DOMAIN
DXLLXXLEXLXXEELKKFKLLLXNXSXXXEXSRIPRXQXX Majority 10 20 30 40	1 FNLOALLIO SODIL SITTITE PAHILOK HKEVD NBS1-PYRIN DOMAIN 1 DHLLST FEU PYDFE FKLOM TYVOK HE STIQ PYRIN-PYRIN DOMIN 1 DALLDALIN TARREST KLISVPLREGYGE GALL CARDS-PYRIN DOMAIN 1 GRLACY FRKKER ELQLELARKAHSRSS GETPAL PECARD7-PYRIN DOMAIN	KADGXXLAXXLVTXYGEXYAVELA LQVLEXMGLRXLA 50 60 70	41 RADGKQ LVEILTHC-DSTWYFMAAS LOTFIKHRMDLS 41 RAPVKMATLLVTYTG EFT QITROTRAINQLLE 41 SMDALDLTDKL SFFLLTGAE TANT RDHULQEM 41 KTSGMEVASYLTAQRTWDLTHTWEQENERSLC

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FIG. 8A

752

ш

LER_RI_2: domain 1 of 8, from 726 to 752: score 0.1,

*->npstretdtsnNklgdeGaraLaeatks<-

HKTVTYLTLQGND-QDDMFPALCEVLRH +++ L L++N+ d+ aL+0+L++

726

NBS1

= 0.031309 ш LBR_RI_2: domain 2 of .8, from 782 to 809: score 20.8, *->npstretdtsnNklgdeGarataeatks<-* NOSLICANLSDNELLDEGAKLLYITLRH n+sL +Ls+N l deGa+ L +L++ 782

FIG. 8B

11 838 [L] LER_RI_2: domain 3 of 8, from 811 to 838: score 21.9, -->npstretdtsnNklgdeGarataeatks<-" KCFLQRLSLENCHLTEANCKDLAAVLVV ** [++[+[+n++]+++ ++ La++] FIG. 8C 811

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895

866 Ш LAR_RI_2: domain 4 of 8, from 839 to 866: score 13.4, -->npstretdtsnNklgdeGarataeatks<-SRELTHLCLAKNPIGNTGVKFLCEGLRY ++ L L L+ N++g G++ L+++L+ 839 NBS1

FIG. 8D

LAR_RI_2: domain 5 of 8, from 868 to 895: score 17.0, E -->npstreidlsnNklgdeGaralaealks<-* **[**[[*n**** +G* [**[**

ECKLQTLVLWNCDITSDGCCDLTKLLQE FIG. 8E

868

NBS1

923 山 LRR_RI_2: domain 6 of 8, from 896 to 923: score 22.6. -->npstretdLsnNklgdeGaraLaeatks<-" KSSLLCLDLGLNHIGVKGMKFLCEALRK ++8T+ LdL+ N++g +G++ L+eaL+ 896 NBS1

FIG. 8F

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0.26 Ħ ш LRR_RI_2: domain 7 of 8, from 925 to 952: score 15.8, -->npstretdtsnNklgdeGarafaeatks<-*

++-Lr L+L+++ + + + L++aL+
LCNLRCLWLWGCSIPPFSCEDLCSALSN

928

NBS1

952

FIG. 8G

u LAR_RI_2: domain 8 of 8, from 953 to 979: score 14.0, -->npstretdtsnNklgdeGaraLaeatks<-" -QSLVTLDLGQNPLGSSGVIOMLFETLTC +SL +LdL++N+lg +G++ L e+L+ 953 NBS1

FIG. 8H

PYRINI-PYRIN DOMAIN PYRINI-PYRIN DOMAIN PYRINI-PYRIN DOMAIN PYRIN-PYRIN DOMAIN PYRIN-PYRIN DOMAIN CARDS-PYRIN Domain CARD7-PYRIN DOMAIN CARDS-PYRIN Domain CARD7-PYRIN DOMAIN CARDS-PYRIN Domain CARD7-PYRIN DOMAIN PYRIN-PYRIN DOMAIN NES1-PYRIN DOMAIN NES1-PYRIN DOMAIN NES1-PYRIN DOMAIN Majority DGVDLATLLVTFY Majority Majority × GLRDL × × EL \mathbb{S} 8 ೫ ш EAM Ø × × × 띠 ᆸ ALALQVL X 0 5 ы 吖 > Δ, × 엵. A ĸ 口 3 ഗ × A W Y EYA LREG G ¥ Ø O S Ē ပါ Ω 4 28 28 28 28 28883

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FIG. 9A

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46 47 **43** 90 90 90 80 80 80 80 80 LANKAHSRSS SGETPA LS VPL REG YG RIPRG YEKAK AARL OKGCIPL FSPAHELOK VPL REG FE MHRM DI VLR DMRMLEE LEDY PP QNTSV INQ AINR MINIC VLR D LOVLRA FNGEE KAWAMAVWIFA AWDUAL S BY LETYGAEL V Q LVASYEDYAKEL TTHCDSYWVEMAS MID GRAR-DA AD H V D L A T L MGTKR-E AGGAWGR A RP V KM TS G MEV MGFN----MOAL **PYPAF1 PYPAF1** CARD7 CARD7 pyrin NBSI POPI ASC POPI

Decoration 'Decoration #1': Shade (with solid black) residues that match the Consensus exactly,

Decoration 'Decoration #2': Shade (with solid black) residues that match the Consensus exactly,

Decoration 'Decoration #3': Box residues that match the Consensus exactly.

9B FIG.

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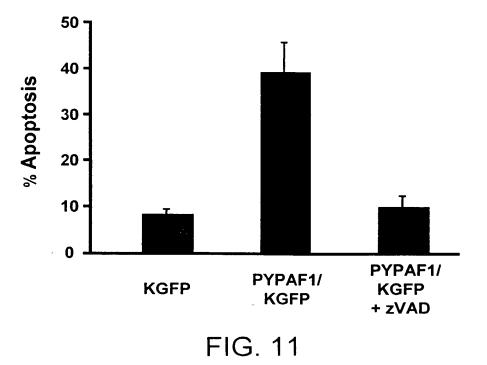
NOVEL MOLECULES OF THE PYRIN DOMAIN PROTEIN

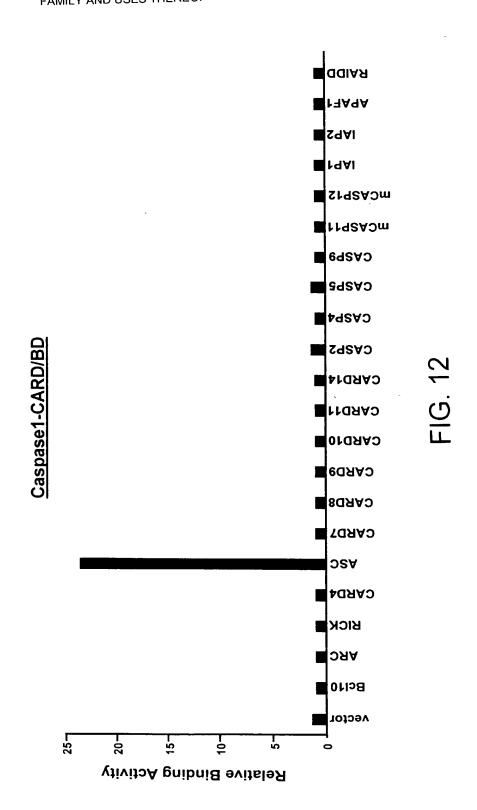
FAMILY AND USES THEREOF

LRR: domain 1 of 9, from 740 to 767: score 10.9, E = 25 FIG. 10A *->nLeeLdLsnN.Lt....slppglfsnLp<-* +L+eLdLs+N+L +++ + +++++ pyrin-1 740 SLTELDLSDNsLGdpgmRVLCETLQHPG **LRR:** domain 2 of 9, from 769 to 796: score 2.3, E = 4.6e+02*->nLeeLdLsnN.Lt....slppglfsnLp<-* FIG. 10B n+++L+L +++L+++ +++ ++s+ + pyrin-1 769 NIRRLWLGRCgLSheccfDISL-VLSSNQ **LRR:** domain 3 of 9, from 797 to 821: score 9.7, E = 39FIG. 10C *->nLeeLdLsnN.Lt..slppglfsnLp<-* +L eLdLs+N L + ++ l+ +L+ pyrin-1 797 KLVELDLSDNaLGdfGIRL-LCVGLK **LRR:** domain 4 of 9, from 826 to 849: score 4.1, E = 2.5e+02*->nLeeLdLsnN.LtslppglfsnLp<-* FIG. 10D nL++L+L ++ Lts +++ pyrin-1 826 NLKKLWLVSCcLTSACCQDLASVL 849 **LRR:** domain 5 of 9, from 854 to 878: score 0.6, E = 8.2e+02*->nLeeLdLsnN.Lt..slppglfsnLp<-* +L++L++ N L ++++ 1+++ + FIG. 10E pyrin-1 854 SLTRLYVGENaLGdsGVAI-LCEKAK 878 **LRR:** domain 6 of 9, from 883 to 906: score 5.1, E = 1.8e+02*->nLeeLdLsnN.LtslppglfsnLp<-* nL++L L n +Lts+ +++s+ FIG. 10F NLQKLGLVNSgLTSVCCSALSSVL pyrin-1 883 **LRR:** domain 7 of 9, from 911 to 935: score 10.2, E = 32*->nLeeLdLsnN.Lt..slppglfsnLp<-* FIG. 10G nL++L+L++N+L ++++ l+++LNLTHLYLRGNtLGdkGIKL-LCEGLL pyrin-1 935 **LRR:** domain 8 of 9, from 940 to 967: score 5.8, E = 1.4e + 02*->nLeeLdLsnN.Lt....slppglfsnLp<-* FIG. 10H +L++L L+n++Lt++ +l+ l+ + + KLQVLELDNCnLTshccwDLST-LLTSSQ pyrin-1 967 **LRR:** domain 9 of 9, from 968 to 991: score 8.4, E = 59*->nLeeLdLsnN.LtslppglfsnLp<-* FIG. 101 +L++L+L nN+L +1 f + pyrin-1 968 SLRKLSLGNNdLGDLGVMMFCEVL 991

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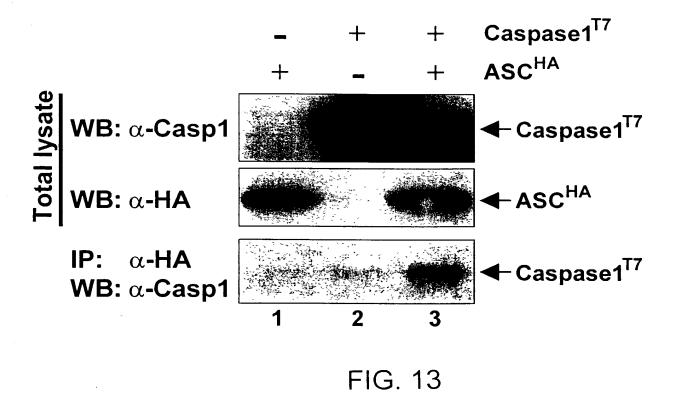
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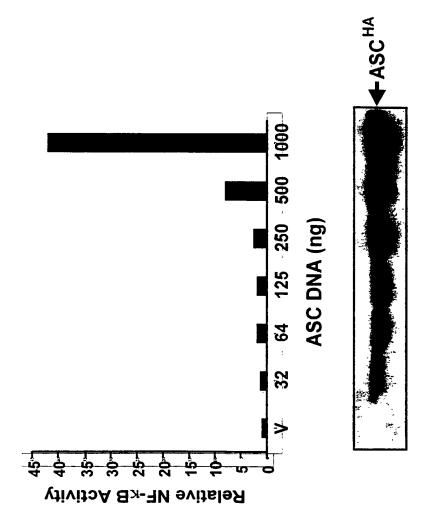




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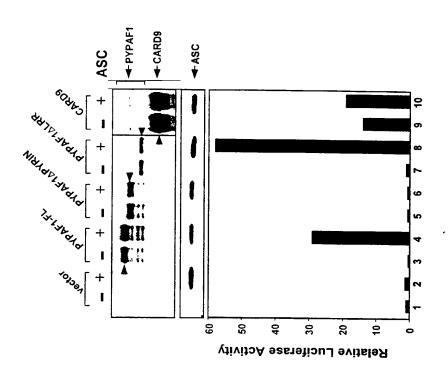
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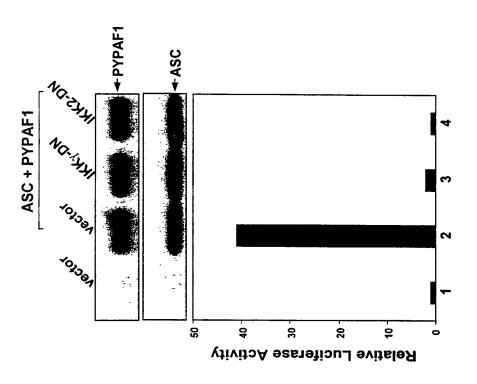
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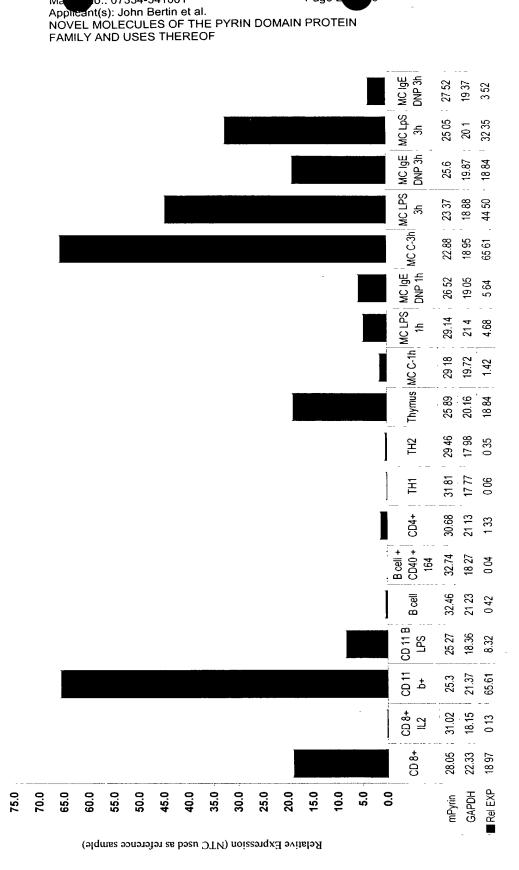


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mPyrin Expression in Normal Mouse Cell Panel



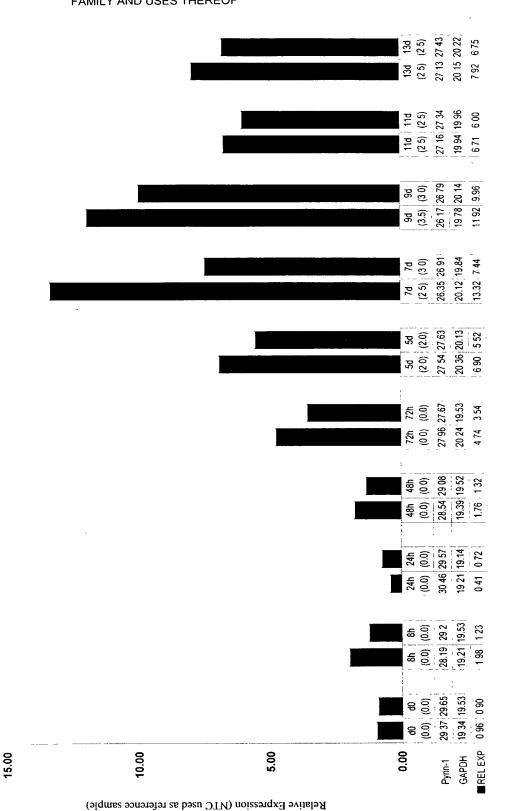
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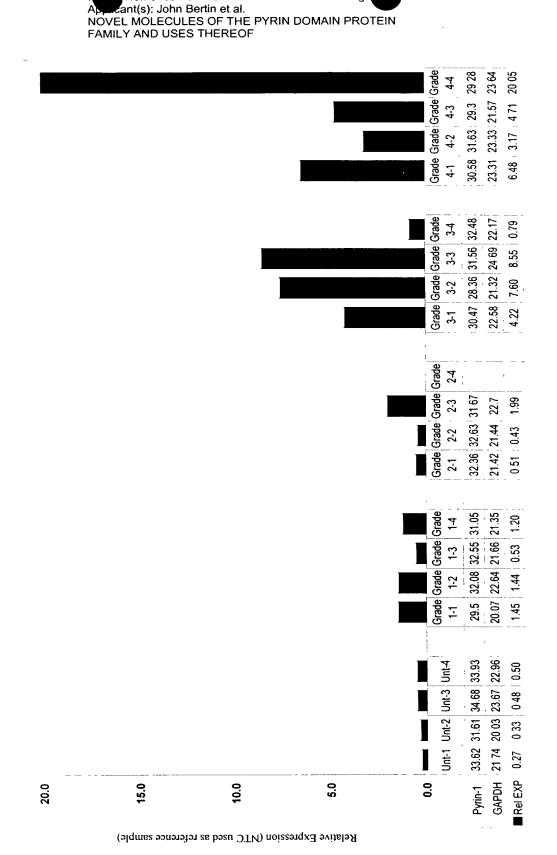
Pyrin-1 Expression in ABT Model

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Pyrin-1 Expression in CIA Model



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